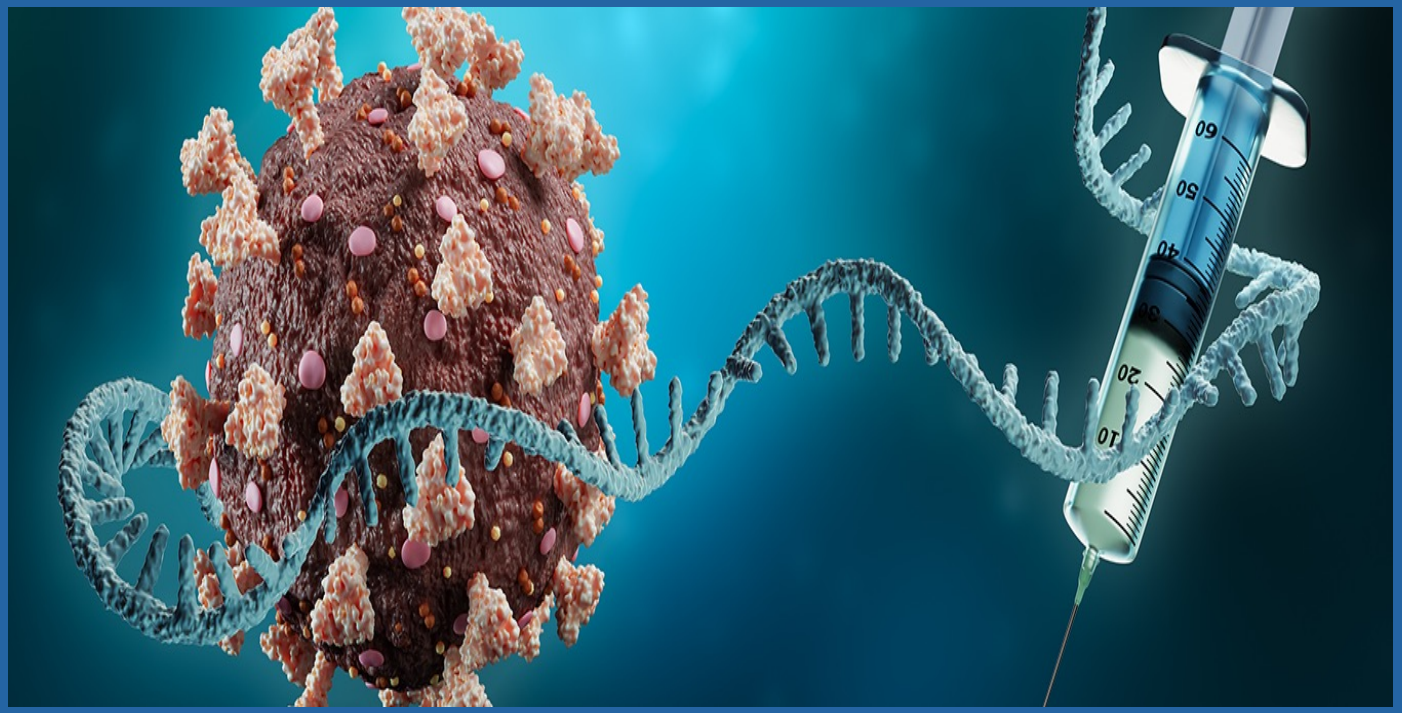
HLA, Vaccines and Viral Immunity



Eric Dorninger ND, LAc

What is HLA?

"The human leukocyte antigen (HLA) system (the major histocompatibility complex [MHC] in humans) is an important part of the immune system and is controlled by genes located on chromosome 6. It encodes cell surface molecules specialized to present antigenic peptides to the T-cell receptor (TCR) on T cells."

"https://www.merckmanuals.com/professional/immunology-allergic-disorders/biology-of-the-immune-system/human-leukocyte-antigen-hla-system"

What is HLA in Plain English?

HLA are our “immune response genetics” from biological mother and father on Chromosome 6 that predict our responses to environmental stimuli.

With Chronic Inflammatory Illnesses, “Genetics loads the Gun, Environment Pulls the Trigger”

Celiac Disease is a Simple Example of HLA Disease Predisposition:

People born with HLA DQ2 and or DQ8 have a higher likelihood of going into Celiac Disease just being born.

If you grow up on the Galapagos islands and eat fish, tubers, bark and berries, you will never express Celiac.

Neverless, the inflammatory expression of Celiac is seemingly more than just Gluten Exposure: “A genetic background (*HLA-DQ2/DQ8* positivity and non-HLA genes) is a mandatory determinant of the development of the disease, which occurs with the contribution of environmental factors (e.g., viral infections and dysbiosis of gut microbiota).”

Ciao, Giamo (2019) Celiac disease: a comprehensive current review BMC Review 17: 142. PMID 31331324

Celiac Disease is a Complicated Example of HLA Disease Predisposition:

"Besides genetic predisposition and exposure to gluten, loss of intestinal barrier function, a pro-inflammatory innate immune response triggered by gluten, inappropriate adaptive immune response, and an imbalanced gut microbiome all seem to be key 'ingredients' of the CD autoimmunity recipe.... innate immunity plays a critical role in initiating CD, and cytokines such as interleukin (IL)-15 and interferon α can prime the innate immune response by polarizing dendritic cells and intraepithelial lymphocyte function"

Ciao, Giamo (2019) Celiac disease: a comprehensive current review BMC Review 17: 142. PMID 31331324

Does HLA effect Vaccines and Viral Immunity?

Don’t sleep on the idea of HLA Immune Response Genetics having major influence on unique, individualized effects to viruses AND/OR their vaccines.

“Narcolepsy, a sleep disorder caused by loss of hypothalamic hypocretin (orexin) neurons is strongly associated with the HLA-DQB1*06:02 genotype and has been thought of as an immune-mediated disease.”

Partinen, Markku (2014) Narcolepsy as an Autoimmune disease: the role of H1N1 infection and vaccination. The Lancet, Vol 13, Issue 6 pp. 600-613 https://doi.org/10.1016/S1474-4422(14)70075-4

Does HLA effect Vaccines and Viral Immunity?

"Results of later studies showed that the HLA-DR2-mediated risk of narcolepsy was controlled by the HLA -QB1*06:02 allele in people of all ethnicities.39, 70 More than 98% of patients with narcolepsy and cataplexy that fulfils strict diagnostic criteria are DQB1*06:02 positive.41, 71 Using less stringent diagnostic criteria, 76–95% of patients with narcolepsy-cataplexy and about 40–60% of patients without cataplexy are DQB1*06:02 positive.72"

Partinen, Markku (2014) Narcolepsy as an Autoimmune disease: the role of H1N1 infection and vaccination. The Lancet, Vol 13, Issue 6 pp. 600-613 https://doi.org/10.1016/S1474-4422(14)70075-4

Does HLA effect Vaccines and Viral Immunity?

"Narcolepsy with cataplexy is tightly linked with two HLA-DQ loci—DQA1*01:02, and DQB1*06:02. Other HLA alleles, such as DQB1*03:01, also affect narcolepsy predisposition, but the effect is weaker.71, 73 Protective alleles of narcolepsy include HLA-DQB1*06:01, DQB1*05:01, DQA1*01 (non-DQA1*01:02), and DQB1*06:03.71, 73 In different ethnic groups most patients (88–98%) with cataplexy are HLA-DQB1*06:02 positive, and only a small proportion of patients with narcolepsy and cataplexy are HLA-DQB1*06:02 negative.41, 71, 73 In narcolepsy without cataplexy, DQB1*06:02 is less common, indicating a different cause."

Partinen, Markku (2014) Narcolepsy as an Autoimmune disease: the role of H1N1 infection and vaccination. The Lancet, Vol 13, Issue 6 pp. 600-613 https://doi.org/10.1016/S1474-4422(14)70075-4

Does HLA effect Vaccines and Viral Immunity?

"After the H1N1 vaccination campaign during the pandemic in 2009–10, a rapid increase in the incidence of narcolepsy was reported, especially in children and adolescents who were vaccinated with AS03 adjuvanted Pandemrix vaccine. Importantly, in controlled epidemiological studies, when individuals who had and who had not been vaccinated with Pandemrix were compared, an increased risk of narcolepsy was noted in vaccinated individuals in many European countries.15, 16, 17, 18, 19, 20, 21, 22 At the same time an increase in incidence was reported from northern China, where the vaccine was not used,23 which suggests that H1N1 virus infection could be an environmental trigger for narcolepsy."

Does HLA effect Vaccines and Viral Immunity?

"Interest in narcolepsy has increased since the epidemiological observations that H1N1 infection and vaccination are potential triggering factors, and an increase in the incidence of narcolepsy after the pandemic AS03 adjuvanted H1N1 vaccination in 2010 from Sweden and Finland supports the immune-mediated pathogenesis. Epidemiological observations from studies in China also suggest a role for H1N1 virus infections as a trigger for narcolepsy. Although the pathological mechanisms are unknown, an H1N1 virus-derived antigen might be the trigger."

Partinen, Markku (2014) Narcolepsy as an Autoimmune disease: the role of H1N1 infection and vaccination. The Lancet, Vol 13, Issue 6 pp. 600-613 https://doi.org/10.1016/S1474-4422(14)70075-4

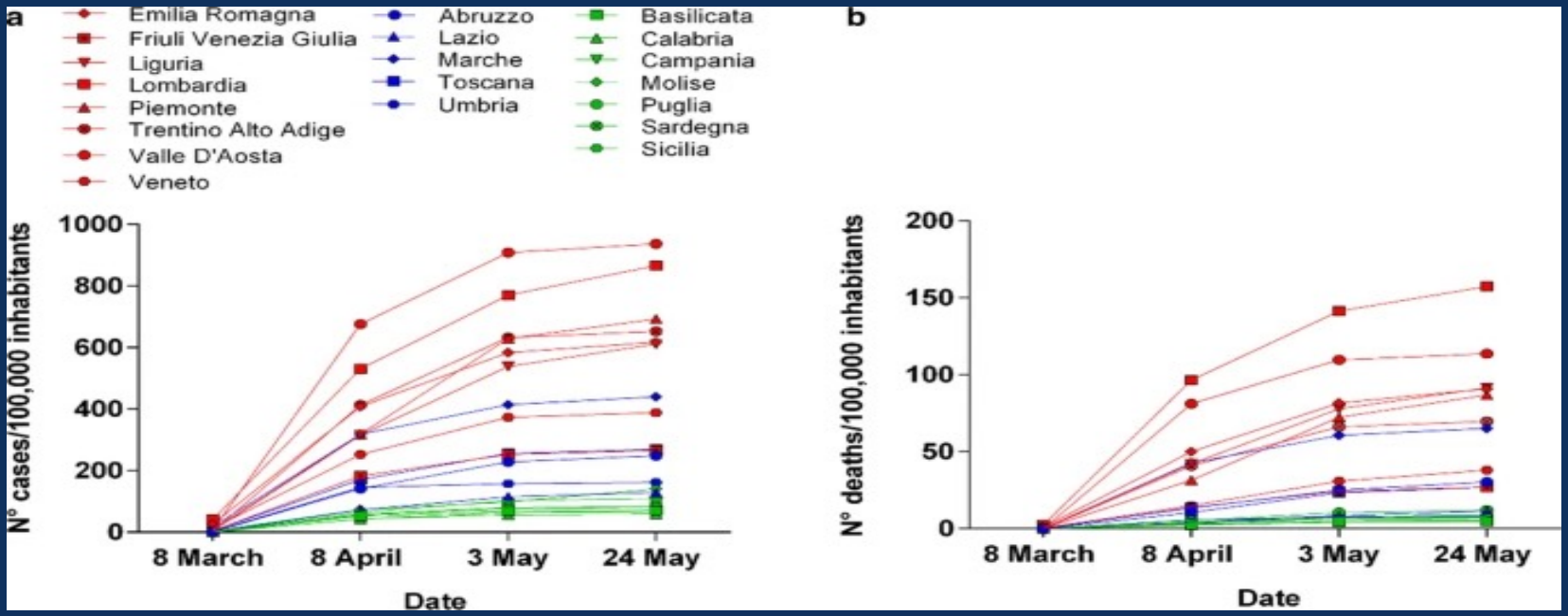
Does HLA effect Vaccines and Viral Immunity?

"In our study HLA-DRB1*04:01 and HLA-DPB1*04:01 occurred at higher frequencies in individuals with seroprotective levels of haemagglutinin antibody.... These alleles are encoded by distinct HLA class II loci, but are relatively common in Caucasoid populations."

Our study demonstrates a significant association between two relatively common HLA class II alleles (DRB1*04:01 and DPB1*04:01) with a higher seroprotective response to trivalent seasonal influenza vaccination in an elderly cohort, and warrants further investigation to validate these observations. Nevertheless, future influenza vaccine trials may need to account for the genetic variability of the target population when evaluating efficacy of vaccine response in elderly or other immuno-compromised and vulnerable groups.

Moss, Alistair J. Correlation between Human Leukocyte Antigen Class II Alleles and HAI Titers Detected Post-Influenza Vaccination. PLoS ONE 8(8): doi:10.1371/journal.pone.0071376

Does HLA Influence Covid Pandemic Incidence and Mortality?



Trend over time relative to the number of Covid-19 cases/100,000 inhabitants and deaths/100,000 inhabitants. The graphs report the number of Covid-19 cases/100,000 inhabitants (**a**) and deaths/100,000 inhabitants (**b**) at four time points of the epidemic. Red symbols are used for northern regions, blue symbols for central regions and green symbols for southern regions

Pisanti, S. (2020), **Correlation of the two most frequent HLA haplotypes in the Italian population to the differential regional incidence of Covid-19,** *Journal of Translational Medicine* **volume 18**, Article number: 352

Does HLA Influence Covid Pandemic Incidence and Mortality?

"We found that the haplotype ranked #1 HLA-A*01:01g-B*08:01g-C*07:01g-DRB1*03:01g shows a positive (suggestive of susceptibility) significant correlation with both Covid-19 incidence and mortality.

Conversely, the haplotype ranked #2 HLA-A*02:01g-B*18:01g-C*07:01g-DRB1*11:04g shows a negative correlation (suggestive of protection). This correlation is observed at all significant time points of the epidemic except for the 8th of March when the numbers were still too low."

Pisanti, S. (2020), **Correlation of the two most frequent HLA haplotypes in the Italian population to the differential regional incidence of Covid-19,** *Journal of Translational Medicine* **volume 18**, Article number: 352

Does HLA Influence Covid Pandemic Incidence and Mortality?

”For the haplotype #1 HLA-A*01:01g-B*08:01g-C*07:01g-DRB1*03:01g, the distribution is characterized by a net clustering of the regions in three groups, with the northern regions reporting high frequency values and corresponding highest incidence and mortality, the central regions displaying intermediate values and the southern regions the lowest values for the haplotype #1 (Fig. 3).”

“On the contrary, for the #2 HLA-A*02:01g-B*18:01g-C*07:01g-DRB1*11:04g haplotype the regions are inversely clustered in three groups, with the southern regions reporting higher frequencies for the haplotype and low numbers of both cases and deaths, whereas central and northern regions show respectively intermediate and low frequencies and progressively increasing reported incidence and mortality of Covid-19 ”.

Pisanti, S. (2020), **Correlation of the two most frequent HLA haplotypes in the Italian population to the differential regional incidence of Covid-19,** *Journal of Translational Medicine* **volume 18**, Article number: 352

Does HLA Influence Covid Pandemic Incidence and Mortality?

"The HLA system affects clinical outcomes in multiple infectious diseases, including HIV and SARS (23, 24). For the latter, population studies observed correlations between certain HLA alleles and the incidence and severity of SARS (24–26). HLA-B*07:03, B*46:01, DRB1*03:01, DRB1 *12:02 alleles were correlated with SARS susceptibility (27, 28). The SARS-CoV-2 sequence displays considerable homology with SARS, but the two viruses do have distinct variations (29). Therefore, it will require further investigation to incorporate HLA alleles when analyzing COVID-19 outcomes (27, 30, 31)"

"....the genetic variability of the MHC molecules can affect the susceptibility and severity of SARS-CoV-2 (35)..... HLA-B*46:01 is expected to have the fewest possible binding peptides for SARS-CoV-2, indicating that individuals with this allele could be especially vulnerable to COVID-19, as had previously been seen for SARS."

"HLA-B*15:03, on the other hand, demonstrated the greatest ability to present highly conserved SARS-CoV-2 peptides shared among common human coronaviruses, indicating that this allele may allow cross-protective T-cell dependent immunity (30). This is a more intriguing mechanism, as HLA-B*1503 appears to be prevalent in West Africa and most countries with high endemic malaria in the World Health Organization(WHO) African Region (37)."

Tavasolian, Fataneh (2021) **HLA, Immune Response, and Susceptibility to COVID-19** Front.Immunol., https://doi.org/10.3389/fimmu.2020.601886

Does HLA Influence Covid Pandemic Incidence and Mortality?

"The clinical course of infection with SARS-CoV-2 is strongly dependent on the relationship between the virus and the host immune system, in which the host HLA plays a central role in the activation and regulation of the immune response. There is scope for further study into the role of HLA in COVID-19, and epidemiological studies need to focus on HLA profiles as host immune determinants. Such studies should include HLA typing of COVID-19 patients, both to unravel the complexity of the disease response and also to inform customized therapies."

"In addition, a prior history of coronavirus infection in the patient can be relevant to the magnitude of the immune response to the current SARS-CoV-2 infection, a phenomenon referred to as "original antigenic sin". This concept refers to cross-reacting immunity due to past infections of similar coronavirus strains, which must be considered in interpreting immune responses to infections and vaccinations."

Tavasolian, Fataneh (2021) **HLA, Immune Response, and Susceptibility to COVID-19** Front.Immunol., https://doi.org/10.3389/fimmu.2020.601886

How About HLA and Vaccine Injury?

"HLA-A*03:01 is associated with increased risk of fever, chills, and more severe reaction to Pfizer-BioNTech COVID-19 vaccination"

Here, we have queried 17,440 participants in the Helix DNA Discovery Project and Healthy Nevada Project about their reactions to COVID-19 vaccination. Our GWAS (Genetic-Wide Association Studies) identifies an association between severe difficulties with daily routine after vaccination and HLA-A*03:01. This association was statistically significant only for those who received the Pfizer-BioNTech vaccine (BNT162b2; p=4.70E-11), but showed a trending association in those who received the Moderna vaccine (mRNA-1273; p=0.005) despite similar sample sizes for study. In Pfizer-BioNTech recipients, HLA-A*03:01 was associated with a two-fold increase in risk of severe vaccine reactions. The effect was consistent across ages, sexes, and whether the person had previously had a COVID-19 infection. The reactions experienced by HLA-A*03:01 carriers were driven by associations with chills, fever, fatigue, and in general feeling unwell.

Bolze, Alexandre (2021) HLA-A*03:01 is associated with increased risk of fever, chills, and more severe reaction to Pfizer-BioNTech COVID-19 vaccination, MedRxiv, doi: https://doi.org/10.1101/2021.11.16.21266408

How About HLA and Vaccine Injury?

"The researchers sent online surveys to Helix DNA Discovery Project and Healthy Nevada Project participants to ask about their vaccination status and any reactions they might have had following their shots. In particular, they asked about symptoms like injection site pain, fever, chills, and fatigue, and whether and to what degree these symptoms affected participants' ability to go about their daily lives. All participants had previously been analyzed with Helix's Exome+ assay."

"Of the 17,440 respondents, 8,041 said they received the Pfizer/BioNTech and 7,085 the Moderna vaccine, while only 790 reported having received the Johnson & Johnson shot. Most respondents, 62.2 percent, reported vaccination had a mild or no effect on their day-to-day life."

https://www.genomeweb.com/infectious-disease/helix-study-finds-tie-between-hla-allele-side-effects-sars-cov-2-vaccines#.YmXNRS-B1bU

Helix Study Finds Tie Between HLA Allele, Side Effects of SARS-CoV-2 Vaccines

How About HLA and Vaccine Injury?

"However, 8.0 percent reported being unable, or only able with extreme difficulty, to perform their daily routines, while 9.6 percent said they had severe difficulties with going about their day."

"In a genome-wide association study comparing participants with extreme or severe difficulties to those with mild or no difficulties, the researchers homed in on a link between HLA-A*03:01 and difficulties with daily routine after vaccination, though this effect was almost entirely driven by the Pfizer/BioNTech vaccine."

"Right now, it's obviously important to reach the largest number of people, and we don't have time or information to do personalization," Fellay said. "But the goal, as in other sectors of medicine, is to try and go in the direction of more stratification or personalization."

https://www.genomeweb.com/infectious-disease/helix-study-finds-tie-between-hla-allele-side-effects-sars-cov-2-vaccines#.YmXNRS-B1bU

Helix Study Finds Tie Between HLA Allele, Side Effects of SARS-CoV-2 Vaccines

Vaccines, A Gray Area with an HLA History: "The Lyme vaccine: a cautionary tale"

People living in endemic areas acquire Lyme disease from the bite of an infected tick. This infection, when diagnosed and treated early in its course, usually responds well to antibiotic therapy. A minority of patients develops more serious disease, particularly after a delay in diagnosis or therapy, and sometimes chronic neurological, cardiac, or rheumatological manifestations.

In 1998, the FDA approved a new recombinant Lyme vaccine, LYMErix™, which reduced new infections in vaccinated adults by nearly 80%. Just 3 years later, the manufacturer voluntarily withdrew its product from the market amidst media coverage, fears of vaccine side-effects, and declining sales. This paper reviews these events in detail and focuses on the public communication of risks and benefits of the Lyme vaccine and important lessons learned.

Nigrovic, L.E. (2007) The Lyme vaccine: a cautionary tale Epidemiol Infect. 2007 Jan; 135(1): 1–8 doi: 10.1017/S0950268806007096

Vaccines, A Gray Area with an HLA History: "The Lyme vaccine: a cautionary tale"

"B. burgdorferi causes a multi-system, multi-stage inflammatory process in infected individuals. Lyme disease typically begins with an expanding skin lesion, erythema migrans, often accompanied by non-specific symptoms including fever, myalgias, and fatigue. If untreated, patients may develop neurological, cardiac, or musculoskeletal complaints. In the chronic phase, large-joint arthritis predominates. Rarely, *B. burgdorferi* infection may be asymptomatic [5]. Some patients complain of chronic musculoskeletal pain, neurocognitive difficulties or fatigue, referred to as 'post-Lyme disease syndrome', which may last for many years after appropriate treatment [6]. Lyme disease rarely, if ever, leads to mortality."

NB. "LYMErix™, which reduced new infections in vaccinated adults by nearly 80%"

Nigrovic, L.E. (2007) The Lyme vaccine: a cautionary tale Epidemiol Infect. 2007 Jan; 135(1): 1–8 doi: 10.1017/S0950268806007096

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In the early 1990s, two different Lyme vaccines emerged that both used the recombinant *B. burgdorferi* surface protein called outer-surface protein A (OspA) as the immugen: LYMErix™ (SmithKlineBeecham, Pittsburgh, PA, USA) and ImuLyme™ (PasteurMérieuxConnaught, Swiftwater, PA, USA). Although researchers recognized the known genetic variability in the OspA within the *B. burgdorferi* strains [16, 17], they chose the most common OspA protein as a target. The OspA vaccines proved effective in animal models and safe in human volunteers [18].

Nigrovic, L.E. (2007) The Lyme vaccine: a cautionary tale Epidemiol Infect. 2007 Jan; 135(1): 1–8 doi: 10.1017/S0950268806007096

Vaccines, A Gray Area with an HLA History: "The Lyme vaccine: a cautionary tale"

Both manufacturers conducted clinical trials in a race to gain the first license for their vaccine [19, 20]. In the LYMErix™ phase III safety and efficacy trial, researchers enrolled 10 906 subjects between 15 and 70 years old who lived in endemic areas and randomized them to receive either the three-dose Lyme vaccine regimen or placebo injections.

Vaccinated individuals showed a 76% reduction in Lyme disease in the year following vaccination [20], with no significant side-effects noted. Based on these promising findings, the U.S. Food and Drug Administration (FDA) approved LYMErix™ on 21 December 1998. Although ImuLyme™ underwent a similar phase III study, the manufacturer, for unpublicized reasons, did not apply to the FDA for licensure [21].

Nigrovic, L.E. (2007) The Lyme vaccine: a cautionary tale Epidemiol Infect. 2007 Jan; 135(1): 1–8 doi: 10.1017/S0950268806007096

Vaccines, A Gray Area with an HLA History: "The Lyme vaccine: a cautionary tale"

At the same time, laboratory investigators started to gain a better molecular understanding of Lyme arthritis. Following infection with *B. burgdorferi*, people with the human leukocyte associated antigen (HLA) type DR4+ genotype (*HLA-DRB1*0401*) might experience increased risk of developing chronic treatment-resistant arthritis.

These findings suggested that, in patients with the DR4+ genotype, an immune response against OspA could translate into a cross-reactive autoimmune response. By implication, an OspA Lyme vaccine might result in autoimmunity in these genetically predisposed individuals. Although causality proved difficult to demonstrate, one study reported four male patients with the DR4+ genotype who developed autoimmune arthritis after receiving LYMErix™ vaccine [34].

Nigrovic, L.E. (2007) The Lyme vaccine: a cautionary tale Epidemiol Infect. 2007 Jan; 135(1): 1–8 doi: 10.1017/S0950268806007096

Vaccines, A Gray Area with an HLA History: “The Lyme vaccine: a cautionary tale”

Differential genetic susceptibility applied to immunization risk represents a new concept. Although the clinical importance of the DR4+ genotype to a person receiving an OspA Lyme vaccine remains incompletely understood, some suggest screening recipients for HLA type DR4+ and vaccinating only non-carriers.

However, genetic screening would add significantly to the costs of a vaccination programme, shifting the cost-benefit ratio towards only the patients at the highest risks of acquiring Lyme disease. However, this approach might limit the potential risks from a vaccine with demonstrated ability to provide more good than harm for the majority of the population.

Nigrovic, L.E. (2007) The Lyme vaccine: a cautionary tale Epidemiol Infect. 2007 Jan; 135(1): 1–8 doi: 10.1017/S0950268806007096

Vaccines, A Gray Area with an HLA History: "The Lyme vaccine: a cautionary tale"

LYMErix™ vaccine was released just as the manufacturer of the oral rotavirus vaccine, RotaShield™, was pulled from the market (Fig.). After nearly a decade in clinical trials, RotaShield™ entered the market in August 1998 with the promise of dramatically reducing the burden of disease from rotavirus, the most important cause of childhood infectious diarrhoea worldwide. Several months later both the American Academy of Pediatrics (AAP) and ACIP added the RotaShield™ vaccine to the routine immunization schedule for all infants [40, 41].

With the increase in use, VAERS quickly began receiving rare reports of intussusception, a potentially life-threatening intestinal blockage [26], and subsequent large case-control and population studies confirmed the association [27, 28]. Epidemiological studies suggested that intussusception occurred in 1–2/10 000 vaccinees, and most experts agreed that this potentially life-threatening risk outweighed the protection against childhood diarrhoea. Consequently in October 1999, 14 months after licensure, the manufacturer withdrew the vaccine [25].

Nigrovic, L.E. (2007) The Lyme vaccine: a cautionary tale Epidemiol Infect. 2007 Jan; 135(1): 1–8 doi: 10.1017/S0950268806007096

Is Immune modulation of Inflammation the Path to safely Heal one Global Nation?

An inflammatory cytokine signature predicts COVID-19 severity and survival:

"Several studies have revealed that the hyper-inflammatory response induced by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a major cause of disease severity and death. However, predictive biomarkers of pathogenic inflammation to help guide targetable immune pathways are critically lacking. We implemented a rapid multiplex cytokine assay to measure serum interleukin (IL)-6, IL-8, tumor necrosis factor (TNF)-α and IL-1β in hospitalized patients with coronavirus disease 2019 (COVID-19) upon admission to the Mount Sinai Health System in New York. Patients (n = 1,484) were followed up to 41 d after admission (median, 8 d), and clinical information, laboratory test results and patient outcomes were collected."

Is Immune modulation of Inflammation the Path to safely Heal one Global Nation?

An inflammatory cytokine signature predicts COVID-19 severity and survival:

Notably, when adjusting for disease severity, common laboratory inflammation markers, hypoxia and other vitals, demographics, and a range of comorbidities, IL-6 and TNF-α serum levels remained independent and significant predictors of disease severity and death.

These findings were validated in a second cohort of patients (n = 231).

We propose that serum IL-6 and TNF-α levels should be considered in the management and treatment of patients with COVID-19 to stratify prospective clinical trials, guide resource allocation and inform therapeutic options.

Del Valle, DM (2020) **An inflammatory cytokine signature predicts COVID-19 severity and survival Nature Mdicine,**Oct;26(10):1636-1643. doi: 10.1038/s41591-020-1051-9.

Tools for Modulating IL-6 and TNF- alpha

WIM HOF BREATHING:

Healthy volunteers were randomized to either the intervention (*n* = 12) or control group (*n* = 12). Subjects in the intervention group were trained for 10 d in meditation (third eye meditation), breathing techniques (i.a., cyclic hyperventilation followed by breath retention), and exposure to cold (i.a., immersions in ice cold water). The control group was not trained. Subsequently, all subjects underwent experimental endotoxemia (i.v. administration of 2 ng/kg *Escherichia coli* endotoxin). In the intervention group, practicing the learned techniques resulted in intermittent respiratory alkalosis and hypoxia resulting in profoundly increased plasma epinephrine levels

Plasma concentrations of proinflammatory cytokines TNF-α, IL-6, and IL-8, and the anti-inflammatory cytokine IL-10 all markedly increased after LPS administration in both groups (Fig. 4). However, in trained individuals, TNF-α, IL-6, and IL-8 levels were significantly attenuated, whereas the IL-10 response was greatly augmented compared with the control group (TNF-α, IL-6, and IL-8 levels 53%, 57%, and 51% lower; IL-10 levels 194% higher).

Kox, M. (2014) Voluntary activation of the sympathetic nervous system and attenuation of the innate immune response in humans
doi: 10.1073/pnas.1322174111s

Tools for Modulating IL-6 and TNF- alpha

Vitamin D and COVID-19 Severity and Related Mortality: A Prospective Study in Italy

"We prospectively studied 103 in-patients admitted to a Northern-Italian hospital (age 66.1 ± 14.1 years, 70 males) for severely-symptomatic COVID-19. Fifty-two subjects with SARS-CoV-2 infection but mild COVID-19 symptoms (mildly-symptomatic COVID-19 patients) and 206 subjects without SARS-CoV-2 infection were controls. We measured 25OHD and IL-6 levels at admission and focused on respiratory outcome during hospitalization."

"In our Covid-19 patients, low 25-OH D levels were inversely correlated with high IL-6 levels and were independent predictors of COVID-19 severity and mortality."

Campi, I (2021) Vitamin D and COVID-19 Severity and Related Mortality: A Prospective Study in Italy BMC Inf Dis Jun 14;21(1):566. doi: 10.1186/s12879-021-06281-7

Tools for Modulating IL-6 and TNF- alpha

The impact of vitamin D_3 intake on inflammatory markers in multiple sclerosis patients and their first-degree relatives:

"Venous blood samples were drawn from Healthy Participants (HP, n = 25) and First-Degree Relative Participants (FDRP, n = 25) as control groups and Multiple Sclerosis Participants (MSP, n = 25) before and after eight weeks of supplementation with 50000 IU vitamin D_3. The mRNA expression and plasma concentrations were gauged by using Real-Time PCR and ELISA assay, respectively."

We observed that supplementation with vitamin D_3 had significantly effect in changing plasma levels of IL-27, TGF-β1, IL-17A, IL-10 & IL-6 in MSP group (A), while, only the plasma levels of IL-6, IL-10 & IL-27 in FDRP group (B) and IL-17A & IL-6 in HP group (C) changed.

Hashemi, Reza (2020) **The impact of vitamin D_3 intake on inflammatory markers in multiple sclerosis patients and their first-degree relatives** https://doi.org/10.1371/journal.pone.0231145

Tools for Modulating IL-6 and TNF- alpha

COVID-19 and IL-6: Why vitamin D (probably) helps but tocilizumab might not

A narrative review of published trials examining the effect of Vitamin D administration in COVID-19 patients was conducted, and the theoretical basis for the use of tocilizumab as an IL-6 antagonist was compared with the immunomodulatory effect of Vitamin D on IL-6 production. Four of the six included studies reported a positive effect of Vitamin D on outcomes. While tocilizumab non-selectively blocks both anti-inflammatory and pro-inflammatory actions of IL-6, Vitamin D lowers immune cell IL-6 production, potentially reducing pro-inflammatory effects, but does not specifically target IL-6 receptors, avoiding any deleterious effect on the anti-inflammatory actions of IL-6. Vitamin D may have advantages over tocilizumab as an IL-6 immunomodulator, and, given that it is safe if administered under clinical supervision, there is a strong rationale for its use.

Silberstein, Morry (2021), COVID-19 and IL-6: Why vitamin D (probably) helps but tocilizumab might not Eur J Pharmacol. 2021 May 15; 899: 10.1016/j.ejphar.2021.174031

Creating a Better Model:

Key Points of Today's Discussion:

Reestablish Trust in Public Health through Cost-Effective, Honest Science

Have Practicing Doctors influence Policy and Treatment Guidelines

Reestablishing medical curiosity, getting comfortable with gray area, creating an apolitical, unemotional society (not just medical) that can unriddle the unique and personal complexities of the immune system

HLA Tracking in VAERS and "Severe" Cases of an infection; Gather HLA evaluation in Mild Cases of Diseases and no adverse reaction to vaccine to establish "healthy control group".

Use this Data base for supporting conversations on who will do just fine with vaccines versus the minority established HLA that should sit out

Have Primary Care Offices and Doctors who have established relationships with Patients and their immune system educate , discuss, inform and if appropriate, administer.

Monitor ER/ICU admissions, Death rate, and "Long Covid" data as Primary concerns.